

Four-protein signature accurately predicts lymph node metastasis and survival in oral squamous cell carcinoma

Type: Article

Abstract:

The presence of lymph node (LN) metastasis significantly affects the survival of patients with oral squamous cell carcinoma (OSCC). Successful detection and removal of positive LNs are crucial in the treatment of this disease. Current evaluation methods still have their limitations in detecting the presence of tumor cells in the LNs, where up to a third of clinically diagnosed metastasis-negative (NO) patients actually have metastasis-positive LNs in the neck. We developed a molecular signature in the primary tumor that could predict LN metastasis in OSCC. A total of 211 cores from 55 individuals were included in the study. Eleven proteins were evaluated using immunohistochemical analysis in a tissue microarray. Of the 11 biomarkers evaluated using receiver operating curve analysis, epidermal growth factor receptor (EGFR), v-erb-b2 erythroblastic leukemia viral oncogene homolog 2 (HER-2/neu), laminin, gamma 2 (LAMC2), and ras homolog family member C (RHOC) were found to be significantly associated with the presence of LN metastasis. Unsupervised hierarchical clustering demonstrated expression patterns of these 4 proteins could be used to differentiate specimens that have positive LN metastasis from those that are negative for LN metastasis. Collectively, EGFR, HER-2/neu, LAMC2, and RHOC have a specificity of 87.5% and a sensitivity of 70%, with a prognostic accuracy of 83.4% for LN metastasis. We also demonstrated that the LN signature could independently predict disease-specific survival ($P = .036$). The 4-protein LN signature validated in an independent set of samples strongly suggests that it could reliably distinguish patients with LN metastasis from those who were metastasis-free and therefore could be a prognostic tool for the management of patients with OSCC.

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